ISSN 2229-3566
Review Article

IJRAP
www.ijrap.net

BENZIMIDAZOLE: A VERSATILE CHEMICAL ENTITY

P.C Santosh*, S.N. Pandeya, Ashish K. Pathak
Saroj Institute of Technology & Management, Lucknow, U.P, India

Received on: 05/10/11 Revised on: 09/11/11 Accepted on: 20/11/11

***Corresponding author**
Email: pcspharma@gmail.com

ABSTRACT
Benzimidazole is a heterocyclic aromatic organic compound. This bicylic compound consists of the fusion of benzene and imidazole. Benzimidazole in an extention of the well elaborated imidazole system has been used as carbon skeleton for N- heterocyclic carbines. A large variety of 2-substituted benzimidazoles have been found to possess antiulcer, antihelmenthic anti-inflammatory, antispasmodic, antihistaminic, antimicrobial, anticancer, cycloxygenase inhibitor, and HIV-1 reverse transcriptase inhibitor activities.

Keywords: Benzimidazole, Antiulcer Agents, Antihelmenthic, Anti-inflammatory.

INTRODUCTION

All the heterocyclic compounds have a great interest in pharmaceutical chemistry. Out of these heterocyclic compounds the benzfused heterocyclic compound i.e. Benzimidazole and its derivatives have wide variety of biological activities, in addition to that the Benzimidazole have played a very important role in the development of theory in heterocyclic chemistry and also extensively in organic synthesis.[1]

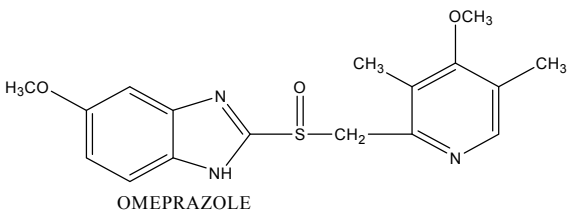
Benzimidazole is an important pharmacophore and privileged structure in medicinal chemistry. Literature survey shows that among the benzimidazole derivatives, 2-substituted ones are found to be pharmacologically more potent and hence the design and synthesis of 2-substituted benzimidazoles are the potential area of research.[2]

Extensive biochemical and pharmacological studies have confirmed that its derivatives are effective against various strains of microorganisms. The reason for a special interest of researchers toward benzimidazole derivatives has been 5,6 dimethyl benzimidazole which is a constituent of naturally occur ring vitamin B12 .Although vitamin B12 is capable of inducing the growth of bacteria, the benzimidazole component and some of its derivatives repress the bacterial growth. Due to the structural similarity to purine, antibacterial ability of benzimidazoles is explained by their competition with purines resulting in inhibition of the synthesis of bacterial nucleic acids and proteins.[2]

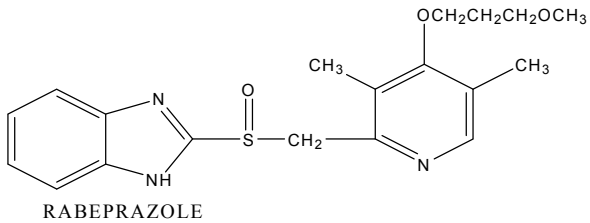
Benzimidazoles drugs are widely used for prevention and treatment of parasitic infections. Thiabendazole (TBZ) was the first benzimidazole to be marketed over 40 years ago. It has been used widely for control of gastrointestinal nematodes, lungworms and as a fungicidal agent. After its introduction, a number of alternative benzimidazoles offering similar activity came to the market, such as parbendazole (PAR), cambendazole (CAM), mebendazole (MBZ) and oxibendazole (OXI). Benzimidazoles possessing sulphide and sulphoxide functional groups were subsequently introduced, offering a wider spectrum of activity and improved efficacy. Albendazole (ABZ), fenbendazole (FBZ) and oxfendazole (OFZ) were the first such benzimidazoles to be successfully used in the treatment of all growth stages of gastrointestinal nematodes. They may be used also in the treatment of lungworms, tapeworms and adult stages of liver fluke. The benzimidazole, triclabendazole (TCB) was later introduced as an antihelmenthic agent for treatment of all stages of liver fluke, but it is ineffective against nematodes. Luxabendazole (LUX) is another benzimidazole-sulphide used in the treatment of food-producing animals but is not licensed for use in the EU. The low solubility of benzimidazole sulphides and sulphoxides leads to their low absorption from the gut, resulting in low bioavailability. Netobimin (NETO) and febantel (FEB),which are the pro-drugs of ABZ and FBZ, respectively, have greater water solubility resulting in improved absorption and increased bioavailability. Similar probenzimidazoles have found widespread use as fungicidal agents, including benomyl (BEN) and thiophanate-methyl (TM), which are precursors of carbendazim (MBC) .

COMPOUNDS HAVING BENZIMIDAZOLE NUCLEUS

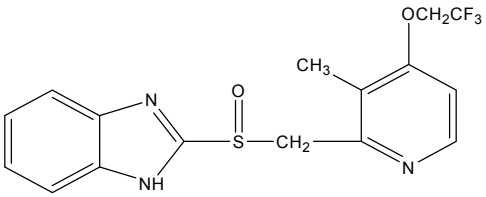
As Antiulcer Agents



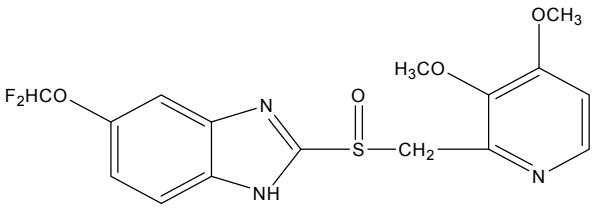
OMEPRAZOLE



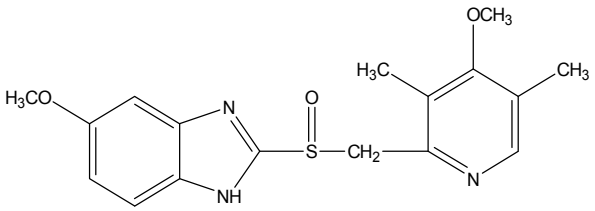
RABEPRAZOLE



LANSOPRAZOLE

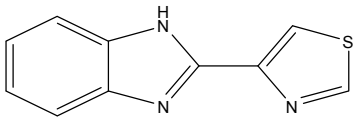


PANTOPRAZOLE



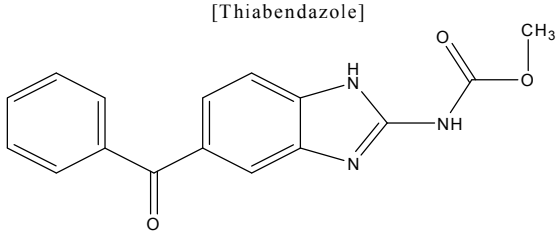
ESOMEPRAZOLE

As Anthelmintic Drugs



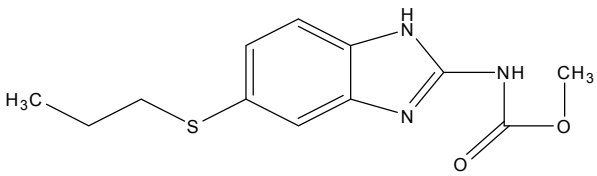
2-Thiazol-4-yl-1*H*-benzimidazole

[Thiabendazole]



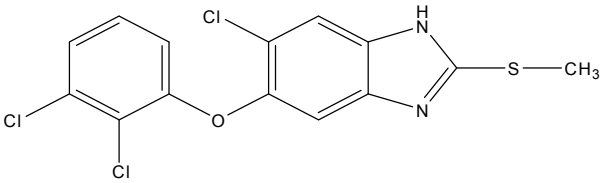
(5-Benzoyl-1*H*-benzoimidazol-2-yl)-carbamic acid methyl ester

[Mebendazole]



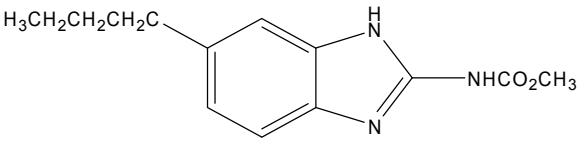
(5-Propylsulfanyl-1*H*-benzoimidazol-2-yl)-carbamic acid methyl ester

[Albendazole]



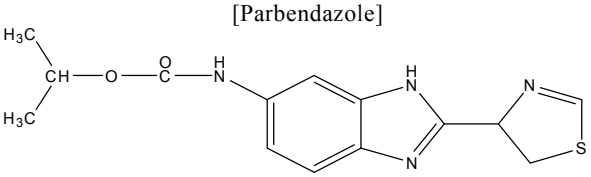
6-Chloro-5-(2,3-dichloro-phenoxy)-2-methylsulfanyl-1*H*-benzoimidazole

[Triclabendazole]



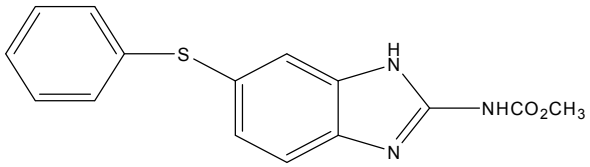
(6-But-3-enyl-1*H*-benzoimidazol-2-yl)-carbamic acid methyl ester

[Parbendazole]



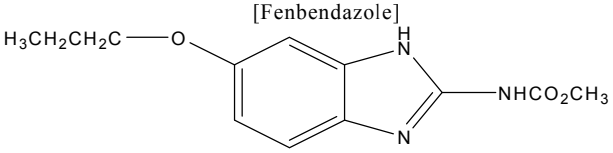
{1-[2-(4,5-Dihydro-thiazol-4-yl)-3,5-dihydro-imidazol-4-ylidenemethyl]-vinyl}-carbamic acid isopropyl ester

[Cambendazole]



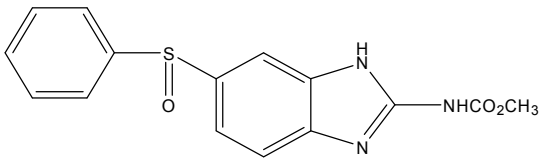
(6-Phenylsulfanyl-1*H*-benzoimidazol-2-yl)-carbamic acid methyl ester

[Fenbendazole]



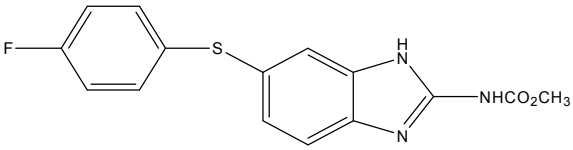
(6-Propoxy-1*H*-benzoimidazol-2-yl)-carbamic acid methyl ester

[Oxibendazole]



(6-Benzenesulfinyl-1*H*-benzoimidazol-2-yl)-carbamic acid methyl ester

[Oxfendazole]



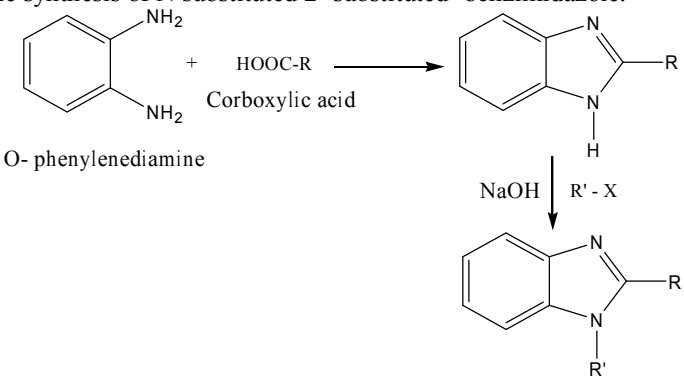
[6-(4-Fluoro-phenylsulfanyl)-1*H*-benzoimidazol-2-yl]-carbamic acid methyl ester

[Luxabendazole]

LITERATURE REVIEW

Chemical Review

A.K. Tiwari et al. (2005) reported the synthesis of N substituted 2- substituted- benzimidazole. [4]



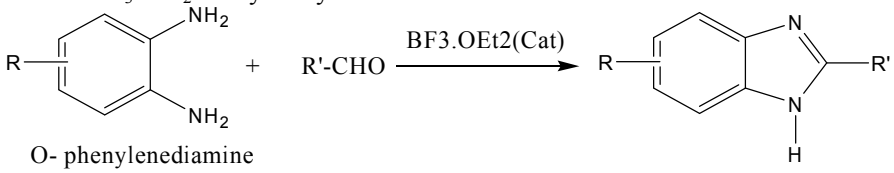
O- phenylenediamine

Corboxylic acid

N-Substituted-2-subsyituted benzimidazole

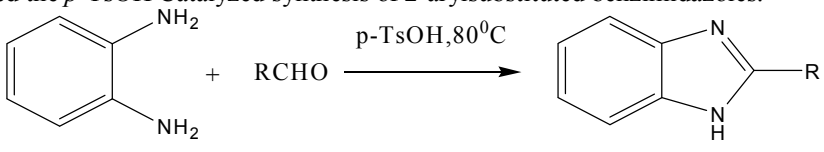
R=CH_2CH_2COOH; R'= $-CH_2C_6H_5$

Nagawade et al. (2006) reported the $BF_3.OEt_2$ catalyzed synthesis of benzimidazole. [5]



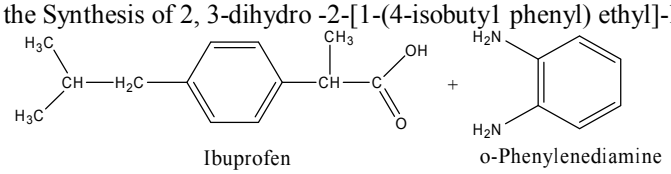
O- phenylenediamine

Wang Yulu et al. (2007) reported the *p*-TsOH Catalyzed synthesis of 2-arylsubstituted benzimidazoles. [6]



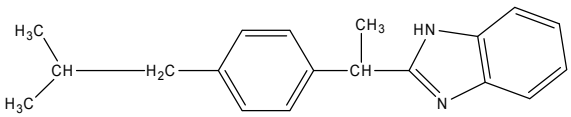
O- phenylenediamine

A. Anton Smith et al. (2008) reported the Synthesis of 2, 3-dihydro -2-[1-(4-isobuty1 phenyl) ethyl]-lH benzo[d] Imidazole. [7]



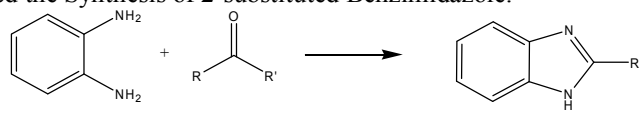
Ibuprofen + o-Phenylenediamine

10%KOH
Heat 2 Hr



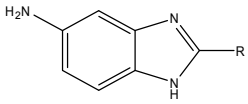
2-[1-(4-Isobutyl-phenyl)-ethyl]-1*H*-benzoimidazole

Jat Rakesh Kumar et al. (2006) reported the Synthesis of 2-substituted Benzimidazole. [8]



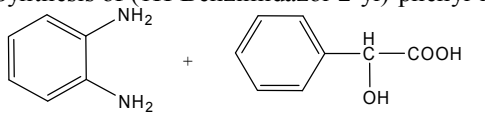
o- Phenylenediamine + R=Alkyl/Aryl, R'= -OH, Acid, R'=H, Aldehyde → 2-substituted Benzimidazole

HNO3
H2SO4



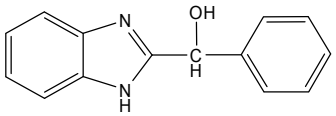
5-Nitro-2-phenyl Benzimidazole

Mukesh C. Sharma et al. (2010) reported the Synthesis of (1H-Benzimidazol-2-yl)-phenyl-methanol. [9]



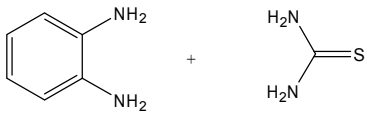
o- Phenylenediamine + Hydroxy-phenyl-acetic acid

4NHCl



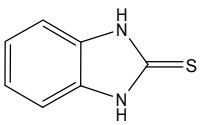
(1*H*-Benzoimidazol-2-yl)-phenyl-methanol

Anoop Singh et al. (2010) reported the synthesis of benzimidazole-2-thione. [10]



o- Phenylenediamine + Thiourea

DMF

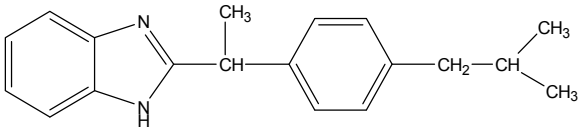


Benzimidazole-2-thione

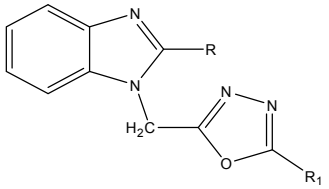
Biological Review

Antimicrobial Activity

A. Anton Smith et al. (2008) reported the synthesis of 2, 3-dihydro-2-[1-(4-isobuty1-phenyl) ethyl]-lHbenzo[d] Imidazole was evaluated for its antimicrobial activity against *S. aureus*, *E. coli, P. aeruginosa.*[7]

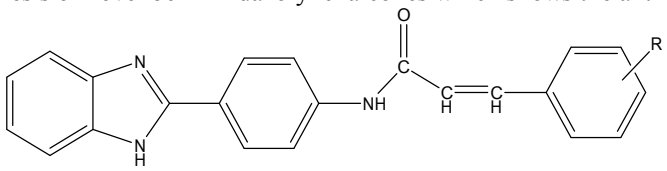


K.F. Ansari *et* al. (2009) reported the synthesis of benzimidazole derivatives having oxadiazole nucleus which shows the antimicrobial activity.[11]



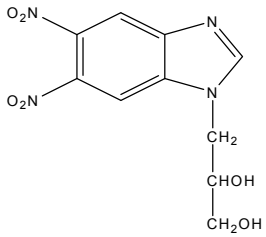
(R=H or CH_3); R1= $-CH_3$, $-C_2H_5$, $-CH_2Cl$, $-CH_2CH_2Cl$, $-C_6H_5$, $2\text{-}ClC_6H_4$

Mishra et al. (2010) reported the synthesis of novel benzimidazolyl chalcones which shows the antimicrobial activity.[12]

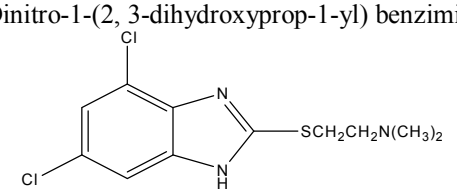


N1-[4-(1H-benzo[d]imidazol-2yl)phenyl]-(E)-3-phenyl-2propenamide,
(R=C6H5)

Mishra et al. (2010) reported the synthesis of nitro and halogeno-substituted benzimidazole derivatives which shows the antimicrobial activity.[12]

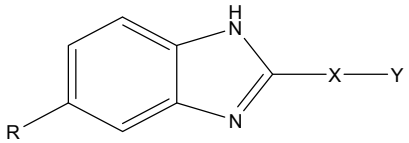


5, 6-Dinitro-1-(2, 3-dihydroxyprop-1-yl) benzimidazole



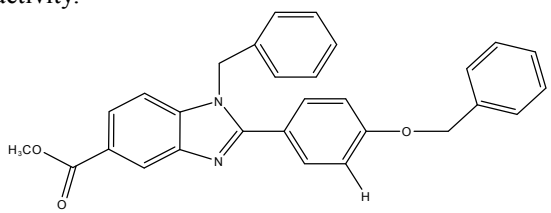
[2-(4,6-Dichloro-1H-benzoimidazol-2-ylsulfanyl)-ethyl]-dimethyl-amine

Mishra et al. (2010) reported the synthesis of some novel 5-substituted benzimidazole derivatives which shows the antimicrobial activity.[12]

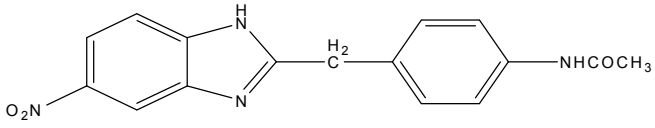


R	X	Y	IUPAC Name
H	-	cyclopentyl	2-Cyclopentyl benzimidazole
Cl	-	cyclopentyl	5-Chloro-2-cyclopentyl benzimidazole
H	CH2	cyclopentyl	2-Cyclopentylmethylbenzimidazole
Cl	CH2	cyclopentyl	5-Chloro-2-cyclopentylmethyl benzimidazole
H	C2H4	cyclopentyl	2-(2 -Cyclopentylethyl) benzimidazole
Cl	C2H4	cyclopentyl	5-Chloro-2-(2-cyclopentylethyl) benzimidazole
H	C2H4	cyclohexyl	5-Chloro-2-(2-cyclohexylethyl) benzimidazole

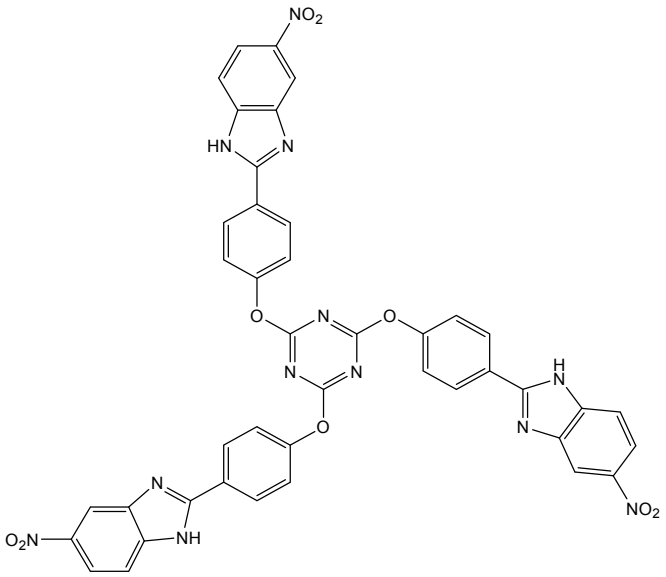
Gulgun Ayhan-Kılcıgil et al. (1999) reported the synthesis of 1-Benzyl-2-(4-benzyloxy-phenyl)-1H-benzoimidazole-5-carboxylic acid methyl ester which shows the antimicrobial activity. [13]



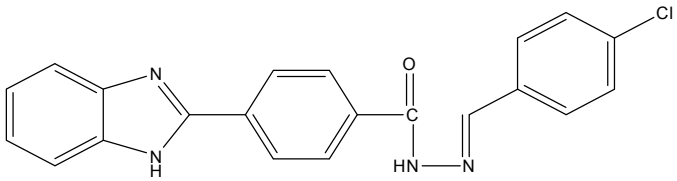
Ismail Yalcın et al. (1998) reported the synthesis of N-[4-(5-Nitro-1H-benzoimidazol-2-ylmethyl)-phenyl]-acetamide which shows the antimicrobial activity. [14]



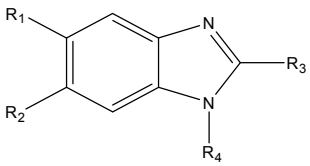
Ziya Erdem Koc et al. (2010) reported the synthesis of tripodal-benzimidazoles which shows the antimicrobial activity. [15]



Yusuf Ozkay et al. (2010) reported the synthesis of 4-(1H-Benzimidazol-2-yl)-benzoic acid (4-chloro-benzylidene)-hydrazide which shows the antimicrobial activity. [16]

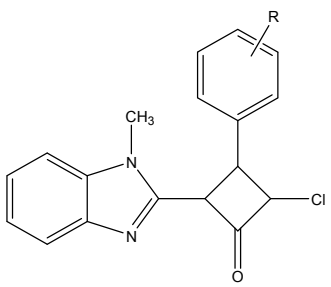


Meral Tuncbilek et al. (2009) reported the synthesis of some novel substituted benzimidazole derivatives having potent activity against MRSA and also showed antifungal activity. [17]



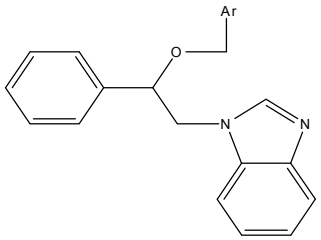
R1	R2	R3	R4	IUPAC Name
Cl	H	H	Cyclopentyl	5-Chloro-1-cyclopentyl-1H-benzimidazole
Cl	Cl	H	Cyclopentyl	5,6-Dichloro-1-cyclopentyl-1H-benzimidazole
Cl	Cl	Cl	Cyclopentyl	2,5,6-Trichloro-1-cyclopentyl-1H-benzimidazole
Cl	Cl	NHCH(CH3)2	Cyclopentyl	5,6-Dichloro-1-cyclopentyl-2-(isopropylamino)-1Hbenzimidazole
Cl	Cl	Br	Cyclopentyl	2-Bromo-5,6-dichloro-1-cyclopentyl-1H-benzimidazole
Cl	Cl	NH2	Cyclopentyl	2-Amino-5, 6-dichloro-1-cyclopentyl-1H- benzimidazole
Cl	H	NH2	Cyclopentyl	2-Amino-5-chloro-1-cyclopentyl-1H-benzimidazole

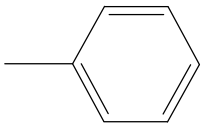
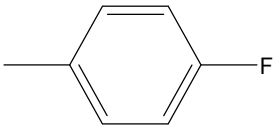
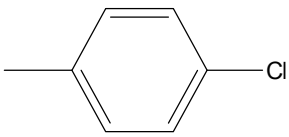
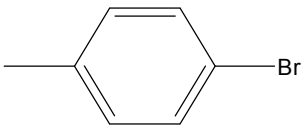
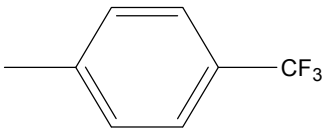
Malleshappa Noolvi et al. (2011) reported the synthesis of antimicrobial and cytotoxic activity of novel azetidine-2-one derivatives of 1H-benzimidazole. [18]



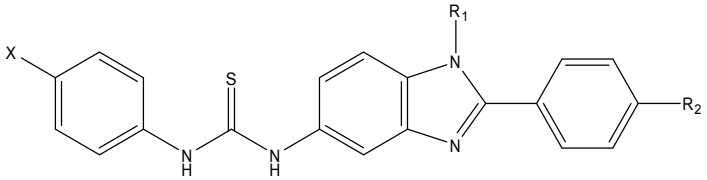
R	IUPAC Name
4-Chloro	3-Chloro-4-(4-chlorophenyl)-1-(1-methyl-1H-benzimidazol- 2-yl) azetidin-2-one
4-Nitro	3-Chloro-1-(1-methyl-1H-benzimidazol-2-yl)-4-(4-nitrophenyl) azetidin-2-one
2-Nitro	3-Chloro-1-(1-methyl-1H-benzimidazol-2-yl)-4-(2-nitrophenyl) azetidin-2-one
3-Nitro	3-Chloro-1-(1-methyl-1H-benzimidazol-2-yl)-4-(3-nitrophenyl) azetidin-2-one
N,N-dimethyl amino	3-Chloro-4-[4-(dimethylamino) phenyl]-1-(1-methyl-1H-benzimidazol-2-yl) azetidin-2-one
2,5-dimethoxy	3-Chloro-4-(2,5-dimethoxyphenyl)-1-(1-methyl-1Hbenzimidazol-2-yl) azetidin-2-one
2-Chloro	3-Chloro-4-(2-chlorophenyl)-1-(1-methyl-1H-benzimidazol-2-yl) azetidin-2-one

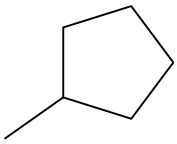
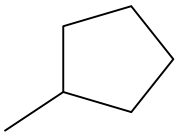
Ozden Ozel Guuven et al. (2011) reported the synthesis and antimicrobial activity of some novel phenyl and benzimidazole substituted benzyl ethers. [19]



Ar	IUPAC Name
	1-(2-(Benzyloxy)-2-phenylethyl)-1H-benzimidazole
	1-(2-(4-Fluorobenzyloxy)-2-phenylethyl)-1H-Benzimidazo
	1-(2-(4-Chlorobenzyloxy)-2-phenylethyl)-1H-benzimidazole
	1-(2-(4-Bromobenzyloxy)-2-phenylethyl)-1H-benzimidazole
	1-(2-(4-(Trifluoromethyl)benzyloxy)-2-phenylethyl)-1Hbenzimidazole

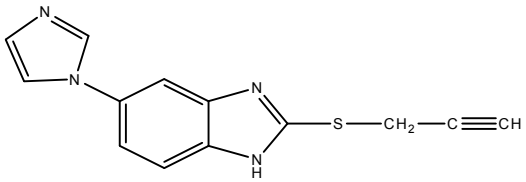
Gulgun Ayhan-Kılcıgil et al. (2006) reported the synthesis of some benzimidazole derivatives and their in vitro antifungal activities were tested against *Candida albicans, Candida glabrata* and *Candida krusei*. Compounds possessed activity comparable to fluconazole against *C. albicans* with a minimum inhibitory concentration of 12.5 g/mL. [13]



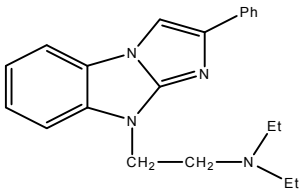
R1	R2	X	IUPAC Name
C3H7	H	H	1-Phenyl-3-(2-phenyl-1-propyl-1H-benzimidazol-5-yl)-thiourea
C3H7	F	Cl	1-(4-Chloro-phenyl)-3-[2-(4-fluoro-phenyl)-1-propyl-1H-benzimidazol-5-yl]-thiourea
	F	H	1-[1-Cyclopenta-1,3-dienyl-2-(4-fluoro-phenyl)-1H-benzimidazol-5-yl]-3-phenyl-thiourea
	F	Cl	1-(4-Chloro-phenyl)-3-[1-cyclopenta-1,3-dienyl-2-(4- fluoro-phenyl)-1H-benzoimidazol-5-yl]-thiourea

Antiulcer activity

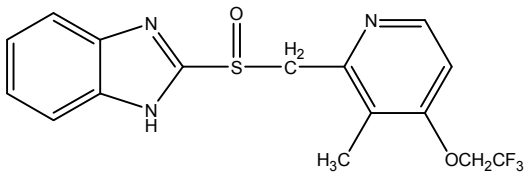
Brumagniez et al. (2008) reported the synthesis of 2-(thiopropyne) - 5- (imidazole -1-yl.) benzimidazole which exhibited moderate antiulcer activity against ulcer induced by anti inflammatory agents in rats orally. [20]



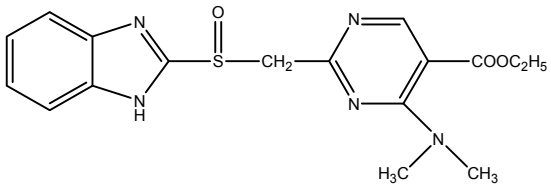
Kovalev et al. (2008) reported the synthesis of 9-(diethyl amino ethylene) 2 – phenyl imidazo [1, 2-a] benzimidazole**,** which was found to be more potent than omeprazole. [20]



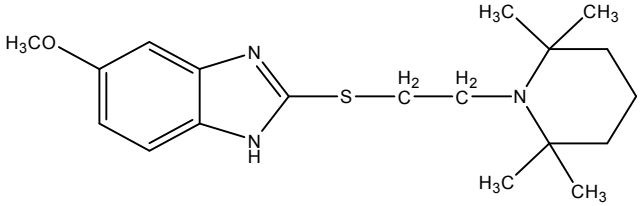
Keiji Kubo et al. (2008) reported the synthesis of 2-[(3-methyl , 4- trifluro ethoxy) 2- pyridyl methyl , sulfinyl] benzimidazole which showed antisecretory, antiulcer , cytoprotective activity. After examining the pharmacological and toxicological properties Lansoprazole was selected as a promising antiulcer agent.[20]



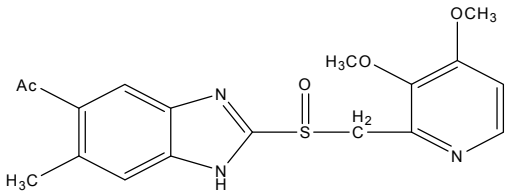
Shimamura et al. (2008) reported the synthesis of 2-[(4-dimethyl amino, 5 carboxylate 2 pyrimidinyl) methyl sulfinyl] benzimidazole in which the pyridine nucleus of omeprazole is replaced by ethyl 4- dimethyl amino-5- pyrimidine carboxylate showed good antiulcer , gastroprotective and antisecretory activity. [20]



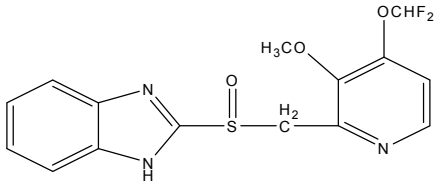
Katano et al. (2008) reported the synthesis of 2 - [(2, 2, 6, 6 tetramethyl piperidine) ethyl thio] 5- methoxy benzimidazole which showed moderate activity. [20]



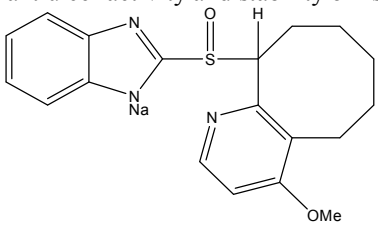
Braendstroem et al. (2008) reported the synthesis of 2- [(3, 4 dimethoxy, 2 –pyridyl) methyl, sulfinyl] 5- acetyl, 6-methyl benzimidazole which inhibited gastric acid secretion in dogs.[20]



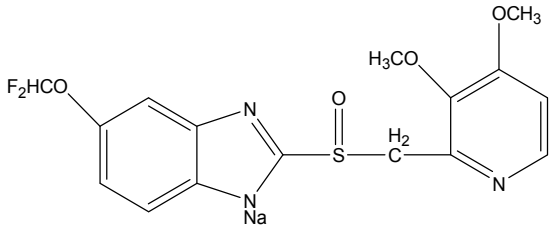
Sohda et al. (2008) reported the synthesis of 2- [(3-methyl, 4-difluromethoxy, 2-pyridyl) methyl, sulfinyl] benzimidazole **inhibited** ethanol induced ulcers in rats.[20]



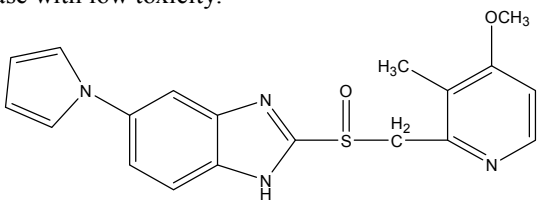
Shin-ichi et al. (2008) reported the synthesis of 2- [(4- methoxy , 6,7,8,9- tetra hydro- 5H – cyclohepta pyridine –9-yl) sulfinyl] 1-H benzimidazole sodium salt which showed promising antiulcer activity and stability on isolated H^+/K^+ -ATPase of rabbit gastric mucosa.[20]



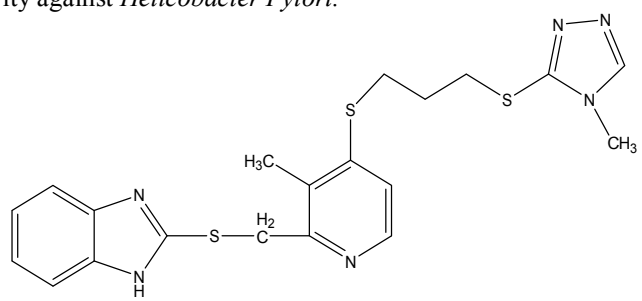
Bernhard et al. (2008) reported the synthesis of 2-[(difluro methoxy-2-pyridyl) methyl sulfinyl] 5- difluromethoxy benzimidazole was highly active against H^+/K^+ -ATPase.[20]



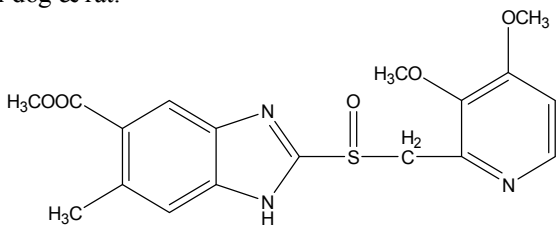
Kim et al. (2008) reported the synthesis of 2-[(3-methyl, 4-methoxy, 2-pyridyl) methyl, sulfinyl 5- (1- pyrrolyl) benzimidazole which showed moderate activity against H^+/K^+ ATPase with low toxicity.[20]



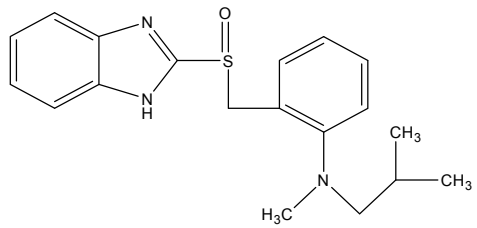
Kohl et al. (2008) reported the synthesis of 2-[3-methyl, 4 (N-methyl, 1, 2, 4 triazole 3 yl, 1, 3 dithiane) 2 pyridyl] methyl thio benzimidazole which showed high activity against *Helicobacter Pylori*.[20]



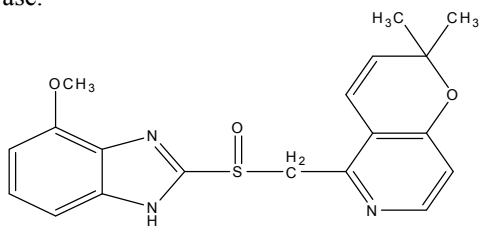
Braendstroem et al. (2008) reported the synthesis of Methyl 2- ((3, 4-dimethoxypyridin-2-yl) methylsulfinyl)-6-methyl-1H-benzimidazole-5-carboxylate **which** showed high activity in dog & rat.[20]



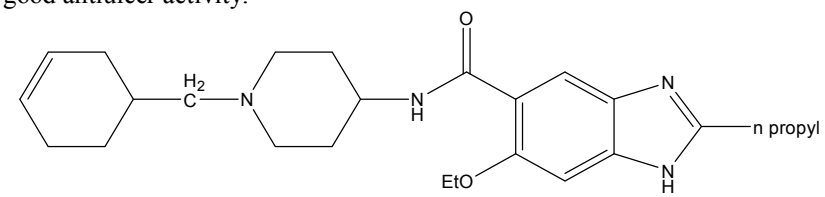
Tsukahara et al. (2008) reported the synthesis of 2- (1-H benzimidazole 2-sulfinyl methyl) phenyl isobutyl methyl amine which showed good antiulcer activity.[20]



Yum et al. (2008) reported the synthesis of 2- [[2,2 dimethyl 2-H pyrrano (3,2,c) 2- pyridyl] methyl, sulfinyl] 4- methoxy benzimidazole which showed high activity against H^+ / K^+ ATPase.[20]

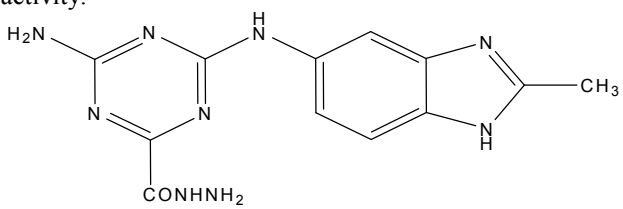


Shrinivasulu et al. (2008) reported the synthesis of 2- n propyl, 5 (N methyl 3, 4 cyclo hexane, 4 amino piperidine) keto, 6 ethoxy, benzimidazole which exhibited good antiulcer activity.[20]

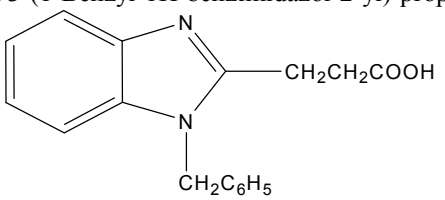


Antiviral Activity

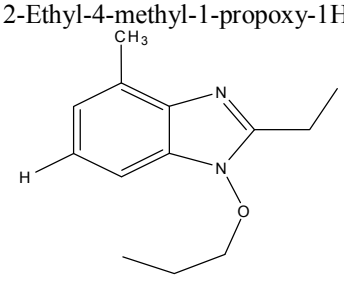
Laila A. Abou-zeid et al. (2008) reported the synthesis of 4-Amino-6-(2-methyl-1H-benzimidazol-5-ylamino)-[1, 3, 5] triazine-2-carboxylic acid hydrazide which shows the antiviral activity. [21]



A.K.Tiwari et al. (2006) reported the synthesis of 3-(1-Benzyl-1H-benzimidazol-2-yl)-propionic acid which shows the antiviral activity. [22]

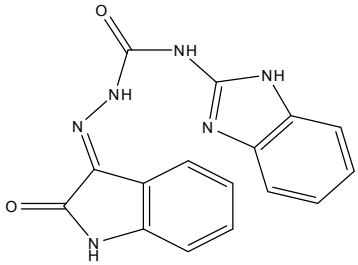


J.M. Gardiner et al. (2006) reported the synthesis of 2-Ethyl-4-methyl-1-propoxy-1H-benzimidazole which shows the antiviral activity. [23]

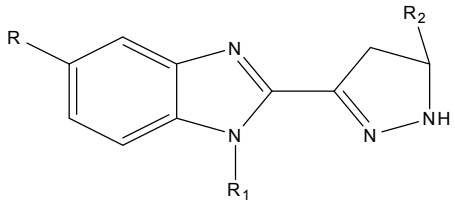


Anti-inflammatory activity

Gummadi et al. (2010) synthesized a series of novel isatinylidene-hydrazinecarboxamide derivatives and evaluated for *in vivo* antiinflammatory activity. [24]



Sawhney et al. (1990) synthesized certain 2-(5-aryl-4, 5-dihydropyrazol-3-yl)- and 2-(2-amino-6-arylpyrimidin-4-yl)benzimidazoles and screened them for antiinflammatory activity.[25]

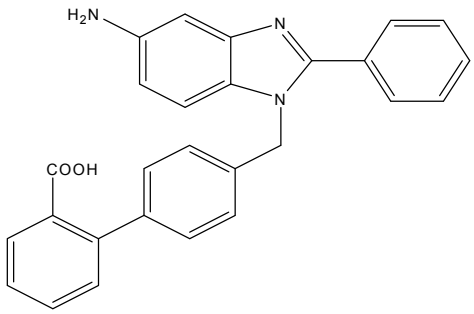


R=H ,NO_2; R1= H, CH_3

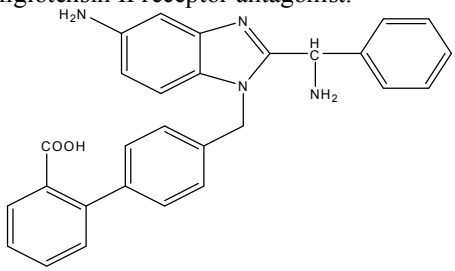
R2= C_6H_5,4-$CH_3C_6H_5$, 4-$CH_3OC_6H_4$,4-ClC_6H_4

Antihypertensive activity

Jat Rakesh Kumar et al. (2006) reported the synthesis of 4'-(5-Amino-2-phenyl-benzimidazol-1-ylmethyl)-biphenyl-2-carboxylic acid which shows the antihypertensive activity. [8]



Mukesh C. Sharma et al. (2010) reported the synthesis of 4'-[5-Amino-2-(amino-phenyl-methyl)-benzoimidazol-1-ylmethyl]-biphenyl-2-carboxylic acid which evaluated for nonpeptide angiotensin II receptor antagonist.[26]



REFERENCES

1. Rishabh D Pandey et al; "Synthesis, characterization and pharmacological screening of novel benzimidazole derivatives", Arabian Journal of Chemistry 10.1016/j.arabjc.2011.04.013.
2. Yusuf Ozkay et al. "Antimicrobial activity and a SAR study of some novel benzimidazole derivatives bearing hydrazone moiety", European Journal of Medicinal Chemistry 2010;45:3293-3298.
3. Mukesh C. Sharma et al., 'Synthesis and biological evaluation of some new benzimidazoles derivatives 4'-{5-amino-2- (2-substituted-phenylamino) phenyl-methyl)-benzimidazol-1ylmethyl}-biphenyl-2-carboxylic acid Nonpeptide angiotensin II receptor antagonists", International Journal of Drug Delivery 2010;2: 265-270.
4. Tiwari A. K. Mishra Anil, "synthesis and antiviral activity of N-substituted -2-substituted benzimidazole derivatives", Ind.J. Of Chem, 2006;45B:489-493.
5. Nagawade, R.Rahul, Shinde,B.Devanand, " $BF_3.OET_2$ Promoted solvent-free synthesis of benzimidazole derivatives", Chinese Chem.Letters, 2006;17(4):453-456.
6. Wang Yulu Han Xiangming, Ma Huiqiang, and "p-TsOH Catalyzed synthesis of 2-arylsubstituted benzimidazoles", Arkivoc, 2007:150-154.
7. A Anton Smith, K Seiyadu Ibrahim , S Parimalakrishnan , A Kottai Muthu, P Muthumani, "Antibacterial and Antifungal Activity of a Benzimidazole Derivative of Ibuprofen", Quarterly j. of applied chem, 2008;1(4):7-12.
8. Jat Rakesh Kumar et al. "Synthesis of Benzimidazole Derivatives: As Anti-hypertensive Agents", E-Journal of Chemistry 2006; 3(13):278-285
9. Mukesh C. Sharma et al., 'Synthesis and biological evaluation of some new benzimidazoles derivatives 4'-{5-amino-2- (2-substituted-phenylamino) phenyl-methyl]-benzimidazol-1ylmethyl}-biphenyl-2-carboxylicacid Nonpeptide angiotensin II receptor antagonists", International Journal of Drug Delivery 2010;2:265-277.
10. Anoop Singh et al , "Synthesis, Biological evaluation, insilico Metabolism and Toxicity prediction of some Novel Benzimidazole-2-thione derivatives", International Journal of PharmTech Research, 2010;2(3):1969-1977
11. K.F. Ansari et al. "Synthesis, physicochemical properties and antimicrobial activity of some new benzimidazole derivatives", European J.of Medicinal Chemistry 2009;44:4028–4033.
12. Mishra et al., "Synthesis and antimicrobial activity of some newer benzimidazole derivatives – an overview", J. of Pharmacy Research 2010; 3(2): 371-37.
13. Gulgun Ayhan-Kılcıgil et al, "Synthesis and antimicrobial activity of some new benzimidazole carboxylates and carboxamides", Farmaco 1999;54:562–565.
14. Ismail Yalcın et al, "Synthesis and antimicrobial activity of some novel 2,5- and/or 6-substituted benzoxazole and benzimidazole derivatives", European Journal of Pharmaceutical Sciences, 1998;7:153–160.
15. Ziya Erdem Koc et al, "Synthesis of novel tripodal-benzimidazole from 2, 4,6-tris(p-formylphenoxy)-1,3,5-triazine: Structural, electrochemical and antimicrobial studies", Journal of Hazardous Materials 2010;183:251–255.
16. Yusuf Ozkay et al. "Antimicrobial activity and a SAR study of some novel benzimidazole derivatives bearing hydrazone moiety", European Journal of Medicinal Chemistry 2010;45:3293-3297.

17. Meral Tuncbilek et al, "Synthesis and in vitro antimicrobial activity of some novel substituted benzimidazole derivatives having potent activity against MRSA", European Journal of Medicinal Chemistry 2009;44:1024–1033.
18. Malleshappa Noolvi et al, "Synthesis, antimicrobial and cytotoxic activity of novel azetidine-2-one derivatives of 1H-benzimidazole", Arabian Journal of Chemistry 2011
19. Ozden Ozel Guuven et al, "Synthesis and antimicrobial activity of some novel phenyl and benzimidazole substituted benzyl ethers", Bioorganic & Medicinal Chemistry Letters 2007;17:2233–2236.
20. Swastika Ganguly, Avinash Patil, and Sanjay Surana, "A systematic review of benzimidazole derivatives as an antiulcer agent", Rasayan J. Chem 2008;1(3):447-460.
21. Laila A. Abou-zeid et al, "Synthesis, Biological Evaluation & Molecular Modeling Investigation of some new Benzimidazole Analogs as Antiviral agents", Saudi Pharmaceutical Journal, 2008;16(2)
22. A.K.Tiwari et al., "Synthesis & antiviral activities of N-substituted-2-substituted-Benzimidazole derivatives", Indian Journal of chemistry, 2006;45-B:489-493.
23. J.M. Gardiner et al, "Synthesis & HIV-1 Inhibition of Novel Benzimidazole Derivatives", Bioorg. & Med. Chem. Lett. 1995;5(12):1251-1252
24. Gummadi et al., "Synthesis, Characterization and Evaluation of Novel N -(1HBenzimidazol-2-Yl)-2-Isatinylidene-Hydrazinecarboxamide Derivatives as Anti Inflammatory Agents", Der Pharma Chemica, 2010;2(3):196-204.
25. Sawhney S.N., Vir. Dharam and Gupta Asha., Indian J. Chem. 1990;29B:1107-1112.
26. Mukesh C. Sharma, Dharm V. Kohli, Smita Sharma, "Synthesis and biological evaluation of some new benzimidazoles derivatives 4'-{5-amino-2-[2-substituted-phenylamino)-phenyl-methyl]-benzimidazol-1 ylmethyl}-biphenyl-2-carboxylic acid: Nonpeptide angiotensin II receptor antagonists", International J of Drug Del 2010;2:265-277.